AMENDMENTS TO THE CLAIMS

In the Claims:

Amendments of claims 1, 11-13, and 15-18, and new claims 26-73 were previously presented in the Amendment filed August 25, 2004. After entering the amendments and new claims presented therein, please amend claim 30, as shown in the following listing of claims, which will replace all prior versions and listings of claims in the application. Claims 2, 4-6, 8, 14, and 20-25 were previously withdrawn without prejudice to the pursuit of these claims in an appropriate divisional or continuation application. Claims 1, 3, 7, 9-13, 15-19, and 26-73 are presently in the application.

Listing of claims:

1 (previously presented). A process for the production of a peptide of interest and pre-sequence having the structure

H-Ala_{10}-Lys-OH

by solid phase synthesis on a solid support, wherein the process comprises:

a. selecting a pre-sequence wherein the pre-sequence is lysine;

b. providing the C-terminal amino acid of the peptide of interest with an N-alpha amino protective group to yield an N-alpha-protected C-terminal amino acid;

c. coupling the pre-sequence lysine to the solid support;

d. coupling the N-alpha-protected C-terminal amino acid to the pre-sequence coupled to the solid support;

e. adding subsequent amino acids forming a peptide sequence by stepwise coupling, or by coupling as a peptide fragment in the form of protected fragments; and

f. removing the protecting groups from the peptide sequence of (d) to yield the peptide of interest.

2 (withdrawn). The process according to claim 1, wherein the presequences have from 5 to 7 amino acid residues.

3 (original). The process according to claim 1, wherein the C-terminal amino acid is side-chain protected.

4 (withdrawn). The process according to claim 1, wherein the amino acids forming part of the presequence are independently selected from the group consisting of Lys, Glu, Asp, Ser, His, Asn, Arg, Met and Gln.

5 (withdrawn). The process according to claim 1, wherein the amino acids in the presequence are either exclusively Lys or Glu or a sequence (Glu)q(Lys)p, where p + q is 3 to 9, and the order of Lys and Glu is arbitrarily chosen.

6 (withdrawn). The process according to claim 1, wherein the amino acids in the presequence are a sequence (Glu)q(Lys)p, where p + q is 6 to 9, and the order of Lys and Glu is arbitrarily chosen.

7 (original). The process according to claim 1, wherein the N-α amino protective group is Fmoc or Boc.

8 (withdrawn).The process according to claim 1, wherein the amino acids in the presequence are chosen from amino acids having a side chain functionality selected from the group consisting of a carboxy, carboxamido, amino, hydroxy, guanidino, sulphide and imidazole moiety.

9 (original). The process according to claim 1, wherein the solid support is a functionalized resin selected from the group consisting of polystyrene, polyacrylamide, polyethyleneglycol, cellulose, polyethylene, latex and dynabeads.

10 (original). The process according to claim 1, wherein the C-terminal amino acid is attached to the solid support by means of a common linker selected from the group consisting of 2,4-dimethoxy-4-hydroxy-benzophenone,4-(4-hydroxymethyl-3-methoxyphenoxy)-butyric acid (HMPB), 4-hydroxymethylbenzoic acid, 4-hydroxymethyl-3-phenoxyacetic acid (HMPA), 3-(4-hydroxymethylphenoxy)propionic acid and p-[(R,S)-α(l-(9H-fluoren-9-yl)-methoxyformamido]-2,4 dimethoxybenzyl)-phenoxyacetic acid.

11 (previously presented). The process according to claim 1, wherein the peptide is cleaved from the solid support by means of an acid, a base or by means of photolysis.

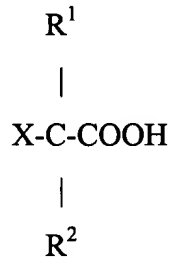
12 (previously presented). The process according to claim 1, wherein the peptide is cleaved from the solid support by means of an acid selected from the group consisting of trifluoroacetic acid (TFA), trifluoromethanesulfonic acid (TFMSA), hydrogen bromide (HBr), hydrogen chloride (HCl) and hydrogen fluoride (HF).

13 (previously presented). The process according to claim 1, wherein the peptide is cleaved from the solid support by means of a base selected from the group consisting of ammonia, hydrazine, an alkoxide and hydroxide.

14 (withdrawn). The process according to claim 1, in which a linker is inserted between the presequence attached to a support and the AA_1-AA_n sequence.

15 (previously presented). The process according to claim 1, in which a linker is inserted between the pre-sequence attached to the solid support and the Ala_{10}, wherein the linker is optically active.

16 (previously presented). The process according to claim 1, in which a linker is inserted between the pre-sequence attached to the solid support and the Ala_{10}, wherein the linker is an α-hydroxy or α-amino acid of the general formula



wherein X is OH or NH_2, and R^1 and R^2 are independently selected from H, C_{1-3} alkyl, phenyl and substituted phenyl, where the substituents are one or more electron donating substituents chosen among C_{1-3} alkoxy, C_{1-3} alkyl, or two vicinal substituent groups are

joined to form a 5 or 6 membered carbon ring together with the carbon atoms to which they are attached.

17 (previously presented). The process according to claim 1, in which a linker is inserted between the pre-sequence attached to the solid support and the Ala_{10}, wherein the linker is (+)-4-methoxymandelic acid, diphenylglycine or glycolic acid.

18 (previously presented). The process according to claim 1, wherein the pre-sequence is enzymatically cleaved from the formed peptide.

19 (original). The process according to claim 18, wherein the enzyme is selected from the group consisting of suitable carboxy- and endopeptidases.

20 (withdrawn). The process according to claim 1, further comprising inserting a first linker between the presequence attached to a support and the AA_1-AA_n sequence and a second linker between the presequence and the solid support with orthogonal cleavage conditions to the first linker so the second linker is selectively cleaved by means of an acid or base to give a peptide AA_1-AA_n linked to the presequence by means of said first linker.

21 (withdrawn). An agent for use in solid phase peptide synthesis having the general formula X-AA'$_1$...-AA'$_m$-Y_1-R, wherein R is a solid support applicable in solid phase peptide synthesis, Y_1 is an amino acid sequence comprising from 3 to 9, independently selected from L-amino acids having a side chain functionality which is protected during the coupling steps and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$, or the corresponding D-amino acid, AA' is an L or D-amino acid residue, m is zero or an integer from 1 to 40 and X is hydrogen or an amino protective group.

22 (withdrawn). An agent for use in solid phase peptide synthesis having the general formula $X\text{-}AA'_1\text{-}. . . \text{-}AA'_m\text{-}L_1\text{-}Y_1\text{-}R$

wherein R is a solid support applicable in solid phase peptide synthesis, Y_1 is an amino acid sequence comprising from 3 to 9, independently selected from L-amino acids having a side chain functionality which is protected during the coupling steps and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$, or the corresponding D-amino acid, AA' is an L or D-amino acid residue, m is zero or an integer from 1 to 40 and X is hydrogen or an amino protective group and L_1 is a linker which enables a selective cleavage of the bond to AA'_m.

23 (withdrawn). An agent for use in solid phase peptide synthesis having the general formula

$X\text{-}AA'_1\text{-----}AA'_m\text{-}L_1\text{-}Y_1\text{-}L_2\text{-}R$

wherein R is a solid support applicable in solid phase peptide synthesis, Y_1 is an amino acid sequence comprising from 3 to 9 amino acid residues independently selected from L-amino acids having a side chain functionality which is protected during the coupling steps and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$, or the corresponding D-amino acid, AA' is an L or D-amino acid residue, m is zero or an integer from 1 to 40 and X is hydrogen or an amino protective group, L_1 is a linker which enables a selective cleavage of the bond to AA'_m and L_2 is a linker with orthogonal cleavage conditions relative to the first linker so that it is selectively cleaved from the solid support.

24 (withdrawn). An agent for use in solid phase peptide synthesis having the general formula

$X\text{-}AA'_1\text{-}.....\text{-}AA'_m\text{-}Y_1\text{-}L_2\text{-}R$

wherein R is a solid support applicable in solid phase peptide synthesis, Y_1 is an amino acid sequence comprising from 3 to 9 amino acid residues independently selected from L-amino acids having a side chain functionality which is protected during the coupling steps and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$, or the corresponding D-amino acid, AA' is an L or D-amino acid residue, m is zero or an integer from 1 to 40 and X is hydrogen or an amino protective group, L_2 is a linker with orthogonal cleavage conditions relative to the first linker and enabling a selective cleavage from the solid support.

25 (withdrawn). An agent for use in solid phase peptide synthesis having the formula

$L_1\text{-}Y_1\text{-}L_2\text{-}R$

Wherein R is a solid support applicable in solid phase peptide synthesis, Y_1 is an amino acid sequence comprising from 3 to 9 amino acids independently selected from L-amino acids having a side chain functionality which is protected during the coupling steps and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$, or the corresponding D-amino acid, L_1 is a linker which enables a selective cleavage of the bond to a peptide sequence and L_2 is a linker with orthogonal cleavage conditions relative to the first linker and enabling a selective cleavage from the solid support.

26 (previously presented). The process according to claim 1, further comprising:

(e) cleaving the pre-sequence from the peptide of interest.

27 (previously presented). A process for the production of a peptide of interest having the structure

$H\text{-}Ala_{10}\text{-}Lys\text{-}OH$

wherein the peptide of interest is C-terminally linked to a pre-sequence Y,

by solid phase synthesis on a solid support, wherein the process comprises:

(a) providing a pre-sequence Y comprising at least one amino acid independently selected from native L-amino acids having a side chain functionality which is protected during the solid phase synthesis and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$ or the corresponding D-amino acids;

(b) providing the C-terminal amino acid of the peptide of interest with an N-alpha amino protective group to yield an N-alpha-protected C-terminal amino acid, wherein the C-terminal amino acid comprises Lys; and

(c) coupling the N-alpha-protected C-terminal amino acid to the solid support, wherein the C-terminal amino acid is C-terminally linked to the pre-sequence Y.

28 (previously presented). The process of claim 27, further comprising:

(d) adding subsequent amino acids forming the peptide sequence by stepwise coupling, or by coupling as a peptide fragment in the form of protected fragments; and

(e) removing the protecting groups from the peptide sequence of (d).

29 (previously presented). The process according to claim 28, further comprising:

(f) cleaving the pre-sequence Y from the peptide of interest.

30 (currently amended). A process for the production of a peptide of interest having the structure

H-Ala_{10}-Lys-Y- OH/NH_2

~~wherein Y is OH, NH_2 or a pre-sequence comprising from 3 to 9 amino acid residues,~~

by solid phase synthesis on a solid support, wherein the process comprises:

a. providing a pre-sequence Y, wherein Y is a pre-sequence peptide comprising ~~at least one amino acid~~ from 3 to 9 amino acid residues independently selected from native L-amino acids having a side chain functionality which is protected during solid phase synthesis and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$ or the corresponding D-amino acids;

b. providing the C-terminal amino acid of the peptide of interest with an N-alpha amino protective group to yield an N-alpha-protected C-terminal amino acid;

c. coupling the pre-sequence Y to the solid support;

d. coupling the N-alpha-protected C-terminal amino acid to the pre-sequence Y coupled to the solid support;

e. adding subsequent amino acids to form a peptide sequence by stepwise coupling, or by coupling as a peptide fragment in the form of protected fragments;

f. removing the protecting groups from the peptide sequence of step d to yield the peptide of interest.

31 (previously presented). The process according to claim 30, further comprising:

g. cleaving the pre-sequence Y from the peptide of interest.

32 (previously presented). The process according to claim 30, wherein the C-terminal amino acid is side-chain protected.

33 (previously presented). The process according to claim 30, wherein the N-α amino protective group is Fmoc or Boc.

34 (previously presented). The process according to claim 30, wherein the solid support is a functionalized resin selected from the group consisting of polystyrene, polyacrylamide, polyethyleneglycol, cellulose, polyethylene, latex and dynabeads.

35 (previously presented). The process according to claim 30, wherein the C-terminal amino acid is attached to the solid support by means of a common linker selected from the group consisting of 2,4-dimethoxy-4-hydroxy-benzophenone,4-(4-hydroxymethyl-3-methoxyphenoxy)-butyric acid (HMPB), 4-hydroxymethylbenzoic acid, 4-hydroxymethyl-3-phenoxyacetic acid (HMPA), 3-(4-hydroxymethylphenoxy)propionic acid and p-[(R,S)-α(l-(9H-fluoren-9-yl)-methoxyformamido]-2,4 dimethoxybenzyl)-phenoxyacetic acid.

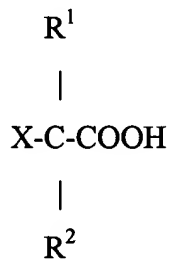
36 (previously presented). The process according to claim 30, wherein the peptide is cleaved from the solid support by means of an acid, a base or by means of photolysis.

37 (previously presented). The process according to claim 30, wherein the peptide is cleaved from the solid support by means of an acid selected from the group consisting of trifluoroacetic acid (TFA), trifluoromethanesulfonic acid (TFMSA), hydrogen bromide (HBr), hydrogen chloride (HCl) and hydrogen fluoride (HF).

38 (previously presented). The process according to claim 30, wherein the peptide is cleaved from the solid support by means of a base selected from the group consisting of ammonia, hydrazine, an alkoxide and hydroxide.

39 (previously presented). The process according to claim 30, in which a linker is inserted between the pre-sequence attached to the solid support and the Ala_{10}, wherein the linker is optically active.

40 (previously presented). The process according to claim 30, in which a linker is inserted between the pre-sequence attached to the solid support and the Ala_{10}, wherein the linker is an α-hydroxy or α-amino acid of the general formula



wherein X is OH or NH_2, and R^1 and R^2 are independently selected from H, C_{1-3} alkyl, phenyl and substituted phenyl, where the substituents are one or more electron donating substituents chosen among C_{1-3} alkoxy, C_{1-3} alkyl, or two vicinal substituent groups are joined to form a 5 or 6 membered carbon ring together with the carbon atoms to which they are attached.

41 (previously presented). The process according to claim 30, in which a linker is inserted between the pre-sequence attached to the solid support and the Ala_{10}, wherein the linker is (+)-4-methoxymandelic acid, diphenylglycine or glycolic acid.

42 (previously presented). The process according to claim 30, wherein the pre-sequence Y is enzymatically cleaved from the formed peptide.

43 (previously presented). The process according to claim 42, wherein the enzyme is selected from the group consisting of suitable carboxy- and endopeptidases.

44 (previously presented). A process for the production of a peptide of interest having the structure

$X\text{-}AA_1\text{-}AA_2\text{.....}AA_n\text{-}Y$

wherein AA is an L or D amino acid residue,

X is hydrogen or an amino protective group,

Y is OH or NH_2 or a pre-sequence comprising from 3-9 amino acid residues,

and n is an integer greater than 2,

by solid phase synthesis on a solid support, wherein the process comprises the following steps:

a. selecting a pre-sequence comprising from 3 to 9 amino acid residues having a side chain functionality which is protected during the solid phase synthesis and

having a propensity factor $P_\alpha > 0.57$ and a propensity factor $P_\beta \leq 1.10$ or the corresponding D-amino acids, wherein the pre-sequence comprises the C-terminal amino acid of the peptide of interest;

b. coupling the pre-sequence Y to the solid support; and

c. providing the C-terminal amino acid of the peptide of interest with an N-alpha amino protective group to yield a N-alpha-protected C-terminal amino acid, coupling the N-alpha-protected C-terminal amino acid to the pre-sequence Y, subsequently N-alpha de-protecting the C-terminal amino acid, whereafter the subsequent amino acids forming a peptide sequence are stepwise coupled or coupled as a peptide fragment in the form of suitably protected derivatives or fragments, wherein the N-alpha-protective group is removed following formation of the peptide of interest, and the peptide is cleaved from the solid support.

45 (previously presented). The process according to claim 44, further comprising:

g. cleaving the pre-sequence Y from the peptide of interest.

46 (previously presented). The process according to claim 44, wherein the C-terminal amino acid is side-chain protected.

47 (previously presented). The process according to claim 44, wherein the N-α amino protective group is Fmoc or Boc.

48 (previously presented). The process according to claim 44, wherein the solid support is a functionalized resin selected from the group consisting of polystyrene, polyacrylamide, polyethyleneglycol, cellulose, polyethylene, latex and dynabeads.

49 (previously presented). The process according to claim 44, wherein the C-terminal amino acid is attached to the solid support by means of a common linker selected from the group consisting of 2,4-dimethoxy-4-hydroxy-benzophenone,4-(4-hydroxymethyl-3-methoxyphenoxy)-butyric acid (HMPB), 4-hydroxymethylbenzoic acid, 4-hydroxymethyl-3-phenoxyacetic acid (HMPA), 3-(4-hydroxymethylphenoxy)propionic acid and p-[(R,S)-α(l-(9H-fluoren-9-yl)-methoxyformamido]-2,4 dimethoxybenzyl)-phenoxyacetic acid.

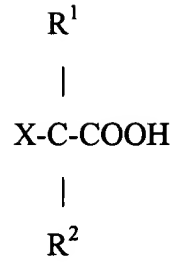
50 (previously presented). The process according to claim 44, wherein the peptide is cleaved from the solid support by means of an acid, a base or by means of photolysis.

51 (previously presented). The process according to claim 44, wherein the peptide is cleaved from the solid support by means of an acid selected from the group consisting of trifluoroacetic acid (TFA), trifluoromethanesulfonic acid (TFMSA), hydrogen bromide (HBr), hydrogen chloride (HCl) and hydrogen fluoride (HF).

52 (previously presented). The process according to claim 44, wherein the peptide is cleaved from the solid support by means of a base selected from the group consisting of ammonia, hydrazine, an alkoxide and hydroxide.

53 (previously presented). The process according to claim 44, in which a linker is inserted between the pre-sequence attached to the solid support and the AA_n, wherein the linker is optically active.

54 (previously presented). The process according to claim 44, in which a linker is inserted between the pre-sequence attached to the solid support and the AA_n, wherein the linker is an α-hydroxy or α-amino acid of the general formula



wherein X is OH or NH_2, and R^1 and R^2 are independently selected from H, C_{1-3} alkyl, phenyl and substituted phenyl, where the substituents are one or more electron donating substituents chosen among C_{1-3} alkoxy, C_{1-3} alkyl, or two vicinal substituent groups are joined to form a 5 or 6 membered carbon ring together with the carbon atoms to which they are attached.

55 (previously presented). The process according to claim 44, in which a linker is inserted between the pre-sequence attached to the solid support and the AA_n, wherein the linker is (+)-4-methoxymandelic acid, diphenylglycine or glycolic acid.

56 (previously presented). The process according to claim 44, wherein the pre-sequence is enzymatically cleaved from the formed peptide.

57 (previously presented). The process according to claim 56, wherein the enzyme is selected from the group consisting of suitable carboxy- and endopeptidases.

58 (previously presented). A process for the production of a peptide of interest comprising more than two amino acid residues C-terminally linked to a pre-sequence, the process by solid phase synthesis on a solid support, wherein the process comprises:

a. selecting a pre-sequence Y comprising at least one amino acid independently selected from native L-amino acids having a side chain functionality which is

protected during the solid phase synthesis and having a propensity factor $P\alpha > 0.57$ and a propensity factor $P\beta \leq 1.10$ or the corresponding D-amino acids;

b. coupling the pre-sequence Y to the solid support;

c. providing the C-terminal amino acid of the peptide of interest with an N-alpha amino protective group to yield an N-alpha-protected C-terminal amino acid; and

d. coupling the N-alpha-protected C-terminal amino acid to the solid support, wherein said C-terminal amino acid is C-terminally linked to the pre-sequence Y.

59 (previously presented). The process according to claim 58, further comprising:

e. removing the N-alpha amino protective group from the N-alpha-protected C-terminal amino acid;

f. adding subsequent amino acids forming a peptide sequence by stepwise coupling, or by coupling as a peptide fragment in the form of protected fragments comprising protecting groups;

g. removing the protecting groups from the peptide sequence of step f to obtain the peptide of interest; and

h. cleaving the peptide of interest from the solid support.

60 (previously presented). The process according to claim 59, further comprising:

i. cleaving the pre-sequence Y from the peptide of interest.

61 (previously presented). The process according to claim 60, wherein the pre-sequence Y is enzymatically cleaved from the formed peptide.

62 (previously presented). The process according to claim 61, wherein the enzyme is selected from the group consisting of suitable carboxy- and endopeptidases.

63 (previously presented). The process according to claim 59, wherein the peptide is cleaved from the solid support by means of an acid, a base or by means of photolysis.

64 (previously presented). The process according to claim 59, wherein the peptide is cleaved from the solid support by means of an acid selected from the group consisting of trifluoroacetic acid (TFA), trifluoromethanesulfonic acid (TFMSA), hydrogen bromide (HBr), hydrogen chloride (HCl) and hydrogen fluoride (HF).

65 (previously presented). The process according to claim 59, wherein the peptide is cleaved from the solid support by means of a base selected from the group consisting of ammonia, hydrazine, an alkoxide and hydroxide.

66 (previously presented). The process according to claim 58, wherein the C-terminal amino acid is side-chain protected.

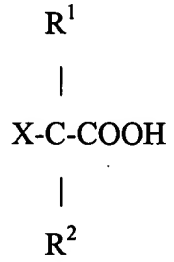
67 (previously presented). The process according to claim 58, wherein the N-α amino protective group is Fmoc or Boc.

68 (previously presented). The process according to claim 58, wherein the solid support is a functionalized resin selected from the group consisting of polystyrene, polyacrylamide, polyethyleneglycol, cellulose, polyethylene, latex and dynabeads.

69 (previously presented). The process according to claim 58, wherein the C-terminal amino acid is attached to the solid support by means of a common linker selected from the group consisting of 2,4-dimethoxy-4-hydroxy-benzophenone,4-(4-hydroxymethyl-3-methoxyphenoxy)-butyric acid (HMPB), 4-hydroxymethylbenzoic acid, 4-hydroxymethyl-3-phenoxyacetic acid (HMPA), 3-(4-hydroxymethylphenoxy)propionic acid and p-[(R,S)-α(1-(9H-fluoren-9-yl)-methoxyformamido]-2,4 dimethoxybenzyl)-phenoxyacetic acid.

70 (previously presented). The process according to claim 58, in which a linker is inserted between the pre-sequence attached to the solid support and the C-terminal amino acid of the peptide of interest, wherein the linker is optically active.

71 (previously presented). The process according to claim 58, in which a linker is inserted between the pre-sequence attached to the solid support and the C-terminal amino acid of the peptide of interest, wherein the linker is an α-hydroxy or α-amino acid of the general formula



wherein X is OH or NH_2, and R^1 and R^2 are independently selected from H, C_{1-3} alkyl, phenyl and substituted phenyl, where the substituents are one or more electron donating

substituents chosen among C_{1-3} alkoxy, C_{1-3} alkyl, or two vicinal substituent groups are joined to form a 5 or 6 membered carbon ring together with the carbon atoms to which they are attached.

72 (previously presented). The process according to claim 58, in which a linker is inserted between the pre-sequence attached to the solid support and the C-terminal amino acid of the peptide of interest, wherein the linker is (+)-4-methoxymandelic acid, diphenylglycine or glycolic acid.

73 (previously presented). A process for the production of a peptide of interest having the structure

H-Ala_{10}-Lys-OH

wherein the peptide of interest is C-terminally linked to a pre-sequence Y,

by solid phase synthesis on a solid support, wherein the process comprises:

(a) providing a pre-sequence Y comprising from 3 to 9 amino acid residues having a side chain functionality which is protected during the solid phase synthesis and having a propensity factor $P_\alpha > 0.57$ and a propensity factor $P_\beta \leq 1.10$ or the corresponding D-amino acids, wherein the pre-sequence comprises the C-terminal amino acid of the peptide of interest;

(b) providing the C-terminal amino acid of the peptide of interest with an N-alpha amino protective group to yield an N-alpha-protected C-terminal amino acid, wherein the C-terminal amino acid comprises Lys;

(c) coupling the N-alpha-protected C-terminal amino acid to the solid support, wherein the C-terminal amino acid is C-terminally linked to the pre-sequence Y;

(d) adding subsequent amino acids forming the peptide sequence by stepwise coupling, or by coupling as a peptide fragment in the form of protected fragments;

(e) removing the protecting groups from the peptide sequence of (d); and

(f) cleaving the pre-sequence Y from the peptide of interest.